REMARKS

In response to the final Office Action of November 17, 2009, applicants submit the following amendments and remarks.

ALLOWABLE SUBJECT MATTER

Applicants would like to thank the Office for the indication of allowability of claim 74, Applicants have amended claim 74 to incorporate the limitations of the base claim 66 and intervening claim 73. The claim should thus be in condition for allowance.

ANTICIPATION REJECTION

On page 2, the Office continued to reject claims 48-55, 57-62, 64-67 under 35 USC 102(b) as being anticipated by Stagljar et al. (PNAS 95:5187-5192, 1998, specifically pp. 5187, 5191 and figure 2; hereinafter "Stagljar").

Applicants previously argued that the bait and prey vectors are maintained episomally and that in contrast, Stagljar's bait vector is integrated into the yeast genome.

While acknowledging that Stagljar's bait vector indeed integrates, the Office now based the anticipation rejection on the definition of the Merriam-Webster online dictionary, which defines the term "episome" as:

> "a genetic determinant (as the DNA of some bacteriophages) that can replicate autonomously in bacterial cytoplasm or as an integral part of the chromosomes."

The Office expressed the opinion that the above definition constitutes the "broadest reasonable interpretation" consistent with the specification for the adjective "episomal".

Applicants noted that the above definition is in fact for the noun "episome." Episomal and episomally are identified as the adjective and the adverb, respectively. "Episomally maintained" is not defined.

Applicants had noted that during patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." Applicants noted in particular that the claims should be given their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004). (MPEP § 2111).

The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999) (MPEP §2111).

The court in *In re Cortright* noted that the "PTO's interpretation of claim terms should not be so broad that it conflicts with the meaning given to identical terms in other patents from analogous art." Id. at 1359.

Applicants previously cited several patents that use the term at issue, namely "maintained episomally." Applicants noted that these patents (analogous art) used the term consistently as the opposite of "integrated."

U.S. Patent **7,435,546** that issued on October 14, 2008 is an example. This patent was examined not only in the same Art Unit (1636) but also by the same Examiner as the present application.

Claim 2 of this patent recites "the first reporter gene and transcriptional regulatory sequence are integrated into the a chromosome . . . or maintained episomally." The specification does not define the term "episomally", but states, among others that "[since] the vector is maintained episomally, the vector can be easily introduced and recovered from a bacterial host cell."

The Office countered applicants' argument by stating that "episomal maintenance was not an issue in US Patent 7,435,546."

Applicants note that the claims, including claim 2, of US Patent 7,435,546 define the property right conferred by this patent. As such "episomal maintenance" is an "issue" in this patent.

However, this patent was cited to show how the "person skilled in the art" would understand this term, a key factor in determining whether the Office's current interpretation of claim term conflicts with "the meaning given to identical terms in other patents from analogous art " See *In re Cortright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999) as cited above.

As noted above, claim 2 of US Patent 7,435,546 states:

> 2. The method of claim 1, wherein the first reporter gene and transcriptional regulatory sequence are integrated into a chromosome of said population of cells or maintained episomally. (*emphasis added*)

If the Examiner had, at the time of examining the claims of US Patent 7,435,546, considered the term "maintained episomally" to be determined by the definition of the noun "episome" as set forth in the Merriam-Webster online dictionary (above), and now cited against applicants' claims, claim 2 of U.S. Patent 7,435,546 should, considering the paradox it poses under the Merriam-Webster online dictionary definition, have been rejected, e.g., as indefinite.

However, instead, the Office apparently took no issue with the expression.

Thus, it appears that the Examiner, at the time US Patent 7,435,546 was prosecuted, interpreted the term "maintained episomally" as others did, e.g. those who wrote and/or examined U.S. Patent **6,902,882** (claims 19 and 20) or **7,608,449** (claims 10 and 11), namely as a opposite to "integrated". It appears that only in the present application, the Examiner gave the term "maintained episomally" a broader meaning in view of the above recited definition of "episome" of the Merriam-Webster online dictionary.

In this context, applicants note that in the context of the term "plasmid construct" (now also part of the claims) the Examiner took yet a different approach to claim interpretation and referred to the use of the term "plasmid" in Stagljar rather than the specification or the Merriam-Webster online Dictionary consulted by the Office for the term "episome." (The Merriam-Webster online Dictionary defines a plasmid as "an extrachromosomal ring of DNA especially of bacteria that replicates autonomously" (*emphasis added*), which well supports applicants' argument of patentability).

Applicants note that the "broadest reasonable interpretation in light of the specification" and the respective interpretation of the claims should, in the least, be applied consistently and objectively, and not vary depending on what interpretation might be best suited to support the Office's obviousness argument.

Applicants also note that the Office, when referring to Stagljar on page page 4, 2nd paragraph, states "…even integrated vectors are maintained episomally," and "[p]lasmids can be integrated into the genome, however, Stagljar teaches plasmids with either a CEN/ARS or 2 micron origin of replication. See, for example, figure 3."

For clarification, the table below lists all vectors described in Stagljar.

As the table clarifies, these vectors:

comprise either a CEN/ARS or 2 micron origin of replication for extrachromosomal replication, or

are integrating vectors and contain no origin of replication.
Furthermore only for prey vectors, Stagljar uses either an episomal vector (pRS314(NubI-ALG5) and pOST1-Nub) or an integrating vector (pRS304(Δost1-Nub)). For bait vectors, Stagljar uses only an integrating vector (pRS305(Δwbp-Cub-PLV)).

Vector in Stagljar	Bait or prey vector	Origin	Extrachromosomal / integrating	Comments
pRS305(Δwbp-Cub-PLV)	Bait	**NONE**	**Integrating**	Page 5188, left column, line 14ff
pRS314(NubI-ALG5)	Prey	CEN/ARS	Extrachromosomal	Page 5188, left column, line 28ff
pRS304(Δost1-Nub)	Prey	**NONE**	**Integrating**	Page 5188, left column, line 42ff
pOST1-Nub	Prey	2micron	Extrachromosomal	Page 5188, right column, line 6ff

OBVIOUSNESS REJECTION

On pages 9 and 10, the Office rejected claims 71 to 73 and 78 to 81 under 35 USC §103(a) as being unpatentable over Stagljar in view of Clarke et al. (hereinafter Clark).

Applicants in particular would like to direct the Office's attention to claim 78 to 81, which recite:

> wherein the bait vector propagates via a CEN/ ARS origin of replication.

Applicants note that the Office acknowledged that Stagljar teaches the CEN/ARS origin of replication only in context of the prey vector NubI-ALG5, but not in the context of a bait vector.

However, the Office referred to Clarke (Ann. Rev. Genet. 19: 29-56, esp. pp- 32-33 (1985)) for use of the CEN/ARS vector as a low copy vector. The Office cited as motivation to combine the teachings of Stagljar and Clarke, Clarke's teaching that the copy number of the CEN/ARS vector is only 1-2 copies per cell and a CEN/ARS vector greatly increases mitotic stability.

The Office, however, did not explain, why the person skilled in the art would use such an origin in a "bait" vector and why a person skilled in the art would like to take the bait vector that has no origin of replication and thus integrates and replace it with a bait vector that has the

specified origin of replication. The Office has in particular also not explained, why the outcome of the combination would produce predictable results (MPEP §2141). Thus, the Office has clearly not supported a *prima facie* case of obviousness.

Consideration of the claims in view of the above comments is respectfully requested.

The Commissioner is authorized to charge any fee deficiencies or overpayments to undersign's deposit account 50-3135.

Respectfully submitted,

By: /Joyce v. Natzmer/
Joyce von Natzmer
Registration No. 48,120
Customer No. 46002
Direct Line: (301) 657-1282

Pequignot + Myers LLC
200 Madison Ave., 1901
New York, NY 10016
Tuesday, January 19, 2010
(first business day after Martin Luther King day)